

related to PWV ($r=.59$ and $.61$, respectively), augmentation index ($r=.53$ and $.56$) and TT/ET ($r=-.60$ and $-.55$) (all $p<.0001$). Age was also significantly related to IRT and E/A ($r=.44$ and $-.68$) (both $p<.0001$), and systolic pressure to IRT ($r=.20$, $p<.05$) and E/A ($r=-.42$, $p<.0001$). In the overall population, augmentation index and TT/ET were significantly related to IRT ($r=.25$ and $-.28$, respectively) and E/A ($r=-.48$ and $.51$) ($p<.001$). PWV was related to IRT and E/A ($r=.36$ and $-.60$, both $p<.0001$). After controlling for PWV, TT/ET and augmentation index, relationships of blood pressure with diastolic function lost any significance and those of age with IRT ($r=.26$, $p<.001$) and E/A ($r=-.44$, $p<.0001$) became weaker.

Conclusion: Both aging and hypertension enhance pressure wave reflection by increasing aortic stiffness. Stronger and earlier RPWs affect relaxation and filling and represent an important functional mechanism of left ventricular diastolic abnormalities.

9:00 a.m.

873-3

Pulse Pressure Is the Best Predictor of Cardiovascular Mortality in 12,763 Middle-Aged Men of the Seven Countries Study: 25-Year Follow-Up

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BACKGROUND: Hypertension is a dominant characteristic in the prediction of cardiovascular disease (CVD). However, much attention has been given over the years to which blood pressure is the best measure for CVD events. The aim of this study was to evaluate the effect of pulse pressure on CVD mortality.

METHODS: Sixteen cohorts of in total 12,763 men aged 40-59 in seven countries (one cohort in the USA, two in Finland, one in the Netherlands, three in Italy, two in Croatia (former Yugoslavia), three in Serbia (former Yugoslavia), two in Greece, two in Japan) were surveyed from 1958 to 1964. Risk factors and personal characteristics were measured and follow-up for vital status and causes of death were carried out over 25 years (1985). Analyses were based on comparisons of mean levels of risk factors and death rates within the 16 cohorts. **RESULTS:** The relation of pulse pressure and 25-year CVD mortality was strongly positive and significant in all cohorts (age adjusted hazard ratio (HR) varied among cohorts from 1.06 to 1.17 per 5 mm Hg, $p < 0.05$). Moreover, statistical analysis (based on Akaike's Information Criterion) revealed that pulse pressure levels were the best predictor for CVD deaths among all blood pressure measurements. This trend was recognizable in normotensive, borderline and sustained hypertensive men, where CVD mortality increased with the level of pulse pressure. Pulse pressure levels were also a significant predictor for coronary heart disease deaths (pooled HR per 5 mm Hg = 1.10, 95% CI 1.08 to 1.11) as well as stroke (pooled HR per 5 mm Hg = 1.13, 95% CI 1.12 to 1.17). **CONCLUSION:** Based on a large, multicultural, population sample of middle-aged men, we revealed that pulse pressure was the best predictor for CVD mortality, among all arterial blood pressures. A potential explanation is that the increase in pulse pressure levels represents the decreased distensibility of the systemic arterial system, which causes the reflect wave to return during ventricular systole.

9:15 a.m.

873-4

Microalbuminuria Predicts Coronary Microvascular Dysfunction in Hypertensive African Americans With Left Ventricular Hypertrophy

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Background: Microalbuminuria (MAL), defined as subclinical elevation of albumin in the urine between 30 to 300 mg/day, is a marker of endothelial dysfunction and, in population studies, has been shown to be an independent predictor of ischemic heart disease. MAL is postulated to occur because of increased microvascular permeability which is caused by circulating inflammatory cytokines or, alternatively, glomerular hypertension. Thus, MAL may be a useful cardiovascular biomarker. The purpose of our study was to examine the correlation between MAL and invasive measures of coronary microvascular function in hypertensive subjects with normal coronary arteries.

Methods: MAL was quantitatively measured in a spot urine collection obtained at the time of the pre-catheterization clinical evaluation. Normal urine albumin concentration is defined as < 2 mg/dl and MAL as 2 to 20 mg/dl. Coronary endothelial function was measured using the Doppler Flowire, quantitative coronary angiography, and the endothelium-dependent and -independent agents, acetylcholine (ACh) and adenosine. The study examined 46 African American (AA) and 58 white (W) hypertensive subjects of similar age, MAP, and BMI with left ventricular hypertrophy (LVH), defined as LV mass indexed by $ht^{2.7} > 47$ g/m $^{2.7}$ in women and > 50 in men.

Results: MAL was present in 19 of 46 AA (41%) and in 14 of 58 W (24%). Both indexed LV mass and MAL were significantly greater in AA (70 ± 2.8 vs 63 ± 2 g/m $^{2.7}$, $p = 0.038$, and 3.0 ± 0.6 vs 1.6 ± 0.4 mg/dl, $p = 0.046$). Peak coronary blood flow (CBF) response to ACh was inversely correlated with MAL concentration among AA ($p = 0.03$, $r = -0.5$) but not among W subjects ($p = 0.51$, $r = -0.19$). Similarly, peak CBF response to adenosine was inversely correlated with MAL among AA ($p = 0.015$, $r = -0.55$), but not among W subjects ($p = 0.22$, $r = -0.35$). Finally, peak CBF response to adenosine, but not ACh, was inversely correlated with MAP among both AA ($p = 0.03$, $r = -0.32$) and W subjects ($p = 0.01$, $r = -0.34$). This appeared to be related, in part, to interaction between MAL and MAP.

Conclusion: We conclude that MAL, in combination with MAP, are useful noninvasive biomarkers for the prediction of coronary microvascular dysfunction, particularly among AA.

873-5

Systolic Reflective Index: A New Parameter to Study Arterial Elasticity

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Background:

Non-invasive techniques to evaluate arterial stiffness include radial artery pulse contour analysis. Diastolic pulse contour analysis provides separate assessment of large artery (C1) and small artery (C2) elasticity. Systolic analysis can identify two pressure peaks (P1 and P2) that relate to incident and reflected waves.

Objective:

To evaluate the relationship between systolic reflective index (SRI, defined as the ratio P2/P1) from systolic pulse contour analysis and C1 and C2, derived from diastolic pulse contour analysis in asymptomatic individuals screened for cardiovascular disease.

Methods:

In 320 subjects (220 male and 100 female healthy subjects with a mean age 51 ± 12 years) radial pulse contour analysis was performed with a piezoelectric transducer and the CVPprofiler-D2020.

Results:

The SRI averaged 0.918 ± 0.059 , C1 16.70 ± 5.80 ml/mm Hg x 10 and C2 6.49 ± 3.21 ml/mm Hg x 100. SRI was inversely related to C2 ($r = -0.590$, $P<0.001$) and to C1 ($r = -0.285$, $P<0.001$). SRI positively related to age ($r = 0.427$, $P<0.001$) and negatively to height ($r = -0.220$, $P<0.001$) and weight ($r = -0.177$, $P<0.001$). There was a weak relationship between SRI and systolic ($r = 0.230$, $P<0.001$) and diastolic blood pressure ($r = 0.130$, $P<0.001$), while there was no relationship with heart rate.

Conclusions:

Systolic Reflective Index (SRI) derived from the systolic part of the radial pulse contour analysis is a useful parameter in the non-invasive assessment of arterial stiffness, which is more influenced by small than large artery elasticity. Diastolic pulse contour analysis provides more insight by separate assessment of the large and small artery elasticity.

9:45 a.m.

873-6

Disparate Effects of Aging on Indices of Aortic Stiffness and Wave Reflection

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Background:

Multiple studies in normal subjects have shown progressive increase in aortic pulse wave velocity (AoPWV) with age, indicating aortic degeneration and stiffening. Such increase is accentuated in patients with hypertension and ischemic heart disease. Studies have also shown increase in late systolic augmentation (Alx) of radial, carotid and aortic pressure waveforms with age. In contrast, preliminary Framingham data, while confirming age increase in AoPWV, shows little increase in carotid Alx with age.

Method:

This study was conducted to explain apparently anomalous findings. A clinical cardiology practice database was interrogated (460 patients, 18-92 years), who were screened for cardiovascular disease or treated for established disease, predominantly atherosclerotic or hypertensive. The vast majority were receiving antihypertensive, vasodilator or anti-anginal therapy. Aortic Alx was determined indirectly using SphygmoCor® from the radial pulse.

Result:

The study population showed less increase in Alx with age ($Alx=0.27(\text{age})+8.8$), than an untreated group ($Alx=0.74(\text{age})-17.1$; Wilkinson et al. Hypertension 2001;38:1461-6) in whom the same technique was used. Thus findings are similar to Framingham, where persons with blood pressure ≥ 140 mmHg were commonly treated with vasodilator drugs, which reduce wave reflection, while having little or no direct effect on aortic stiffness.

Conclusion:

In populations with hypertensive and atherosclerotic disease, increase in aortic stiffness with age can be gauged by AoPWV, but not by Alx, since Alx is modified by drug therapy.